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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/614,037	07/08/2003	Manfred Reiter	14693-0195	9074

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EXAMINER	
VOGEL, NANCY S	

ART UNIT	PAPER NUMBER
1636	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/614,037	REITER ET AL.	
	Examiner	Art Unit	
	Nancy T. Vogel	1636	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *07 August 2007*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *34-36 and 46-48* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *34-36 and 46-48* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Claims 34-36 and 46-48 are pending in the case.

Any rejection of record in the previous action not addressed in this office action is withdrawn.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 34-36 and 46-48 are rejected under 35 U.S.C. 103(a) as being unpatentable over Shibuya et al. (US Patent 6,406,909) (newly cited) in view of Kistner et al. (5,753,489) and Quest International Product Information, Norwich, NY, 1995 and . Sheffield Pharma, (newly cited).

This rejection is maintained essentially for the reasons made of record in the previous Office action, mailed 2/8/07. To recapitulate,

Shibuya et al. disclose a method of culturing animal cells using serum-free medium or components from animals, using soybean protein hydrolysate at 1-5 g per liter, and yeast extract at 1-5 g per liter (col. 2 lines 56-65). The reference discloses that animal cells may be mammalian cells such as CHO, HeLa, BHK, myeloma (col 4 lines 42-48). The reference discloses (col. 8, lines 14-22) the soy hydrolysate may be

Hysoy, which is the same as that disclosed in the instant specification at page 9 [30]. The yeast hydrolysate may be Hy-yest, as is disclosed in the instant specification. The reference discloses that this method of culturing cells using animal protein free medium comprising soy hydrolysate and yeast hydrolysate is advantageous since the cells have increased cultivation efficiency, i.e. higher growth rate and higher rate of production or a recombinant protein or peptide (col. 7 lines 45-55).

The difference between the reference and the instant claims is that the cell culture method has the additional steps of infecting the cells with a virus, incubating the cells to propagate the virus, and harvesting the virus or virus antigen produced. . Furthermore, particular sizes of the molecules in the hydrolysates, i.e. 90% of the molecules in the hydrolysates have a molecule weight of less than or equal to 1000 Daltons, is not disclosed.

However, Kistner et al. disclose a method of producing an immunogenic composition comprising virus or virus antigen, comprising providing a culture of a mammalian cells, infecting the cells with a virus, incubating the culture of cells to propagate the virus, harvesting the virus or antigen, and preparing an immunogenic composition from the virus or antigen (see col. 5-6). The virus may be orthomyxoviridae, paramyxoviridae and reoviridae, and the cells may be vertebrate cells such as VERO, CV-1, LLC-MK2, MDCK, MDBK cells (col. 6, lines 1-15). Quest International Product Information discloses that HY-SOY, which is a well known soy hydrolysate, has 25.4% of molecules less than 200 D, 57.5% in the 200-500 D range, and 16.8% in the 500-1000 D range. The product pages disclose that the hydrolysates

are useful for applications that require high solubility, including microbiological laboratories and in fermentation products requiring a water soluble, vegetable source peptone.. . Furthermore, technical literature from Sheffield Pharma, current makers of such products as "Hy-Soy"™ and "Hy-Yest" ™ also show that the molecular weight distribution of virtually all products is: 90% of molecules are less than 1 kD in size.

It would have been obvious to one of ordinary skill in the art to have included the steps of infecting the cultured cells with a virus of interest, cultivating the infected cells, harvesting the virus, and isolating an immunogenic antigen therefore, as disclosed by Kistner et al., in the method of culturing animal cells disclosed by Shibuya et al., since both references disclose the growth of cells in culture for the purpose of producing virus or recombinant products of interest. . It would have been further obvious to use well known soy or yeast hydrolysates commercially available, such as those disclosed in the Quest International Product Information pages, which are disclosed to be "refined" and to have a molecule weight distribution in which at least 90% of the molecules have a molecule weight of less than or equal to 1000 Daltons. Furthermore, technical literature from Sheffield Pharma, current makers of such products as "Hy-Soy"™ and "Hy-Yest" ™ also show that the molecular weight distribution of virtually all products is: 90% of products are less than 1 kD in size. One would have been motivated to do so by the disclosure of Shibuya et al. that the method avoids contamination by animal proteins, and results in increased cultivation efficiency, and the disclosure of the Quest International product information, which discloses that the hydrolysates are refined and are of low molecular weight, and are useful for applications that require high solubility,

including microbiological laboratories and in fermentation products requiring a water soluble, vegetable source peptone.. Based upon the teachings of the cited references, the high skill of one of ordinary skill in the art, and absent evidence to the contrary, there would have been a reasonable expectation of success to result in the claimed invention.

Applicant's arguments filed 8/7/07 have been considered, but have not been found convincing.

Applicant has argued that Shibuya et al. discloses that an animal protein, i.e. human insulin, is present in the disclosed medium, and therefore, the medium or method disclosed by Shibuya et al. is not "animal protein free". Applicant points for support to Table 1 of Shibuya, et al., which lists human insulin as an ingredient of medium. However, it is maintained that the medium in Table 1 is only an example, and in fact, in the growth medium for the data shown in Fig. 8, no insulin is present. This is the only animal protein in the medium listed in Table 1. Therefore, the medium used for cell growth in the experiment of Fig. 8 does not have any animal derived component. Therefore, the rejection is maintained.

Claims 34-36 and 46-48 are rejected under 35 U.S.C. 103(a) as being unpatentable over Price et al. (WO 98/15614) (cited by applicants)in view of Kistner et al. (US Patent 5,753,489) and Quest International Product Information, Norwich NY, 1995, and Sheffield Pharma Ingredients, Cell Nutrition, Hydrolyzed Proteins & Yeast Extracts, Technical Manual, (newly cited).

To recapitulate:

Price et al. disclose a method of culturing cells comprising providing a culture of cells that have been grown in an animal protein free medium comprising soy hydrolysate at a concentration of about .1% and yeast hydrolysate at a concentration of0.1% to about .8% (pages 19-20). Price et al. disclose this method is useful for culture of animal cells including human cells and kidney cells (see page 24). Price disclose the method may be used to grow and produce viruses using cell culture (page 2).

The difference between the reference and the instant claims is that the steps of infecting the cells with virus, incubating the infected cells to propagate the virus, harvesting the virus and preparing an immunogenic composition, and specifically, conducting those steps using particular viruses, is not disclosed. Furthermore, particular sizes of the molecules in the hydrolysates, i.e. 90% of the molecules in the hydrolysates have a molecule weight of less than or equal to 1000 Daltons, is not disclosed.

However, Kistner et al. disclose a method of producing an immunogenic composition comprising virus or virus antigen, comprising providing a culture of a mammalian cells, infecting the cells with a virus, incubating the culture of cells to propagate the virus, harvesting the virus or antigen, and preparing an immunogenic composition from the virus or antigen (see col. 5-6). The virus may be orthomyxoviridae, paramyxoviridae and reoviridae, and the cells may be vertebrate cells such as VERO, CV-1, LLC-MK2, MDCK, MDBK cells (col. 6, lines 1-15). Quest International Product Information discloses that HY-SOY, which is a well known soy

hydrolysate, has 25.4% of molecules less than 200 D, 57.5% in the 200-500 D range, and 16.8% in the 500-1000 D range. The product pages disclose that the hydrolysates. are useful for applications that require high solubility, including microbiological laboratories and in fermentation products requiring a water soluble, vegetable source peptone.. . Furthermore, technical literature from Sheffield Pharma, current makers of such products as "Hy-Soy"™ and "Hy-Yest" ™ also show that the molecular weight distribution of virtually all products is: 90% of molecules are less than 1 kD in size.

It would have been obvious to one of ordinary skill in the art to have included the steps of infecting the cultured cells with a virus of interest, cultivating the infected cells, harvesting the virus, and isolating an immunogenic antigen therefore, as disclosed by Kistner et al., in the method of cultivating cells disclosed by Price et al., since both references disclose the growth of cells in culture for the purpose of producing virus or recombinant products of interest. It would have been further obvious to use well known soy or yeast hydrolysates commercially available, such as those disclosed in the Quest International Product Information pages, which are disclosed to be "refined" and to have a molecule weight distribution in which at least 90% of the molecules have a molecule weight of less than or equal to 1000 Daltons. Furthermore, technical literature from Sheffield Pharma, current makers of such products as "Hy-Soy"™ and "Hy-Yest" ™ also show that the molecular weight distribution of virtually all products is: 90% of molecules are less than 1 kD in size. One would have been motivated to do so by the disclosure of Price et al. that the method avoids contamination by animal proteins, and the usefulness of the cell culture method for producing virus, and the disclosure of the

Quest International product information, which discloses that the hydrolysates are refined and are of low molecular weight, and are useful for applications that require high solubility, including microbiological laboratories and in fermentation products requiring a water soluble, vegetable source peptone.. Based upon the teachings of the cited references, the high skill of one of ordinary skill in the art, and absent evidence to the contrary, there would have been a reasonable expectation of success to result in the claimed invention.

Applicant's arguments have been considered but have not been found convincing. Applicants have pointed to sections of Price et al. that disclose the addition of certain components derived from animal cells. However, it is maintained that the reference discloses that these components may be added, but does not disclose that they are necessarily present. Therefore, it is maintained that the reference does disclose the animal protein free medium as one possible culture medium.

Conclusion

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of

the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Nancy T. Vogel whose telephone number is (571) 272-0780. The examiner can normally be reached on 7:00 - 3:30, Monday - Friday.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Joseph Woitach can be reached on (571) 272-0739. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

NTV
10/15/07

NANCY VOGEL
PRIMARY EXAMINER